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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,163	SCHALL ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,7-13 and 29-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,7-13 and 29-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10/31/03* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on October 31, 2003 wherein the instant specification has been amended as to page 8 and 10; claims 14-21 are cancelled and claims 5, 7-13, and 29-34 have been amended and claims 35-40 are newly submitted.

Currently, claims 5, 7-13, and 29-40 are pending in this application.

Claims 5, 7-13, and 29-34 as amended now and new claims 35-40 are examined on the merits herein.

Applicant's amendment amending claims 5 and 7-13, filed October 31, 2003 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of enablement in these claims of record stated in the Office Action dated July 29, 2003 has been fully considered and is found persuasive to remove the rejection since the recitation "preventing" has been removed. Therefore, the said rejection is withdrawn.

Applicant's remarks regarding the cancellation of claim 30 of copending Application No. 09/944,049 filed on October 31, 2003 with respect to the rejection of claims 5 and 29 provisionally made under the judicially created doctrine of obviousness-type double patenting of record stated in the Office Action July 29, 2003 have been considered and are found persuasive to remove this particular rejection. Therefore, the said rejection is withdrawn.

The following are new rejection(s) necessitated by Applicant's amendment filed October 31, 2003, wherein the limitations in the amended claims have been changed and new claims are added.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 29 as amended now and new claims 35-40 are rejected under 35 U.S.C. 112, first paragraph, for **scope** of enablement because the specification, while being enabling for the particular compounds of formula disclosed in the specification and for the particular compounds of formula also recited in claim 30 for example employed in the claimed methods herein, does not reasonably provide enablement for the employment of any small organic compounds having a molecular weight of less than 800 daltons and which blocks or inhibits the binding of a chemokine to US28 receptor or a US28 receptor fragment in the particular method for treating CMV infection in a human, for the same reasons of record in the previous Office Action July 29, 2003.

These recitation, "a small organic compound having a molecular weight of less than 800 daltons and which blocks or inhibits the binding of a chemokine to US28 receptor or a US28 receptor fragment", is seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method for treating CMV infection in a human.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claim 29 is deemed very broad since these claims reads on any small organic compounds having a molecular weight of less than 800 daltons and which blocks or inhibits the binding of a chemokine to US28 receptor or a US28 receptor fragment employed in the claimed methods of treatment herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants in claim 29, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997). The CAFC clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise

definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphasis added).

In the instant case, "a small organic compound having a molecular weight of less than 800 daltons and which blocks or inhibits the binding of a chemokine to US28 receptor or a US28 receptor fragment" recited in the instant claims is purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides those particular compounds of formula for the claimed method of treatment herein in claims 30-34.

Thus, Applicants functional language at the points of novelty in claim 29 fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph, since it fails to provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)). The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d

833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, except those particular compounds of formula disclosed in the specification, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any small organic compounds having a molecular weight of less than 800 daltons having claimed functional properties in the claimed method of treatment herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects for treatment of CMV infection in a human, side effects, and especially serious toxicity that may be generated when and/or after administering to a human of any compounds represented by "a small organic compounds having a molecular weight of less than 800 daltons and which blocks or inhibits the binding of a chemokine to US28 receptor or a US28 receptor fragment" in the particular method for treating CMV infection in a human. See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible adverse effects (9th ed, 1996) page 51 and 57-58. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of

adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added).

In the instant case, in the absence of fully recognizing the identity of the members genus herein except those particular compounds of formula in the specification, one of skill in the art would not be able to fully predict the possible treatments herein and possible adverse effects occurring with many compounds having claimed functional properties in the claimed method herein. Thus, the teachings of the "Goodman & Gilman's" book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

It is noted that only two particular compounds octoclothepin and methiothepin were tested in working Examples in the specification. Thus, the evidence in the examples is also not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the active compounds in the claimed method. See MPEP § 716.02(d).

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the

embodiments of any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims to be administered to a human employed in the claimed method of the particular treatments herein, with no assurance of success.

Applicant's remarks with respect to the rejection made under 35 U.S.C. 112 first paragraph of record in the previous Office Action July 29, 2003 have been fully considered and not found persuasive since Applicant's arguments are directed to lack of enablement. However, this rejection is made under 35 U.S.C. 112 first paragraph not for lack of enablement, but for lack of **scope** of enablement of any compounds represented by "a small organic compounds having a molecular weight of less than 800 daltons and which blocks or inhibits the binding of a chemokine to US28 receptor or a US28 receptor fragment" employed in the particular method for treating CMV infection in a human without ***undue experimentation***, as pointed out in the previous Office Action and the set forth rejection above.

Additionally, Applicant's arguments that the methods for screening disseminstion in vivo have been disclosed in the copending Application No. 09/944,049, are not found convincing since the instant claims are not limited to any small organic compound having a molecular weight of less than 800 daltons and which blocks or inhibits the binding of a chemokine to US28 receptor or a US28 receptor fragment, obtained from the methods for screening disseminstion in *vivo* disclosed in the copending Application No. 09/944,049. As noted in MPEP 2111, during patent examination, claims are given their **broadest** reasonable interpretation. It is proper to use the specification to interpret what the applicant meant by a word or phrase recited in the claim, However, it is not proper to read limitations appearing in the specification into the claim when these limitations are not recited in the claim. See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) for example.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 7-13, and 29-34 as amended now and new claims 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Protiva et al. (4,243,805, of record) in view of in view of the Merck Manual of Diagnosis and Therapy (17th ED, of record)

and Michelson ("AT", PTO-1449 submitted May 12, 2003, of record) for the same reasons of record in the previous Office Action July 29, 2003.

Protiva et al. discloses that the compounds of formula (1) which are the instant preferred compounds in claims 7-13 and 30-33, and which are also known small organic compounds having a molecular weight of less than 800 daltons, have psychotropic and neurotropic activity and are useful as neuroleptics (see abstract, col.1-4 in particular).

Protiva et al. does not expressly disclose the employment of the particular compounds in a method for treating CMV infection in a human or slowing the progression of CMV dissemination in the human, and wherein the chemokine is fractalkine.

The Merck Manual of Diagnosis and Therapy (17th ED) teaches that CMV infection is manifested by severe brain damage, CNS damage or CNS involvement in a human. See the right column of page 1295 to the left column of page 1296.

Michelson teaches that CMV infection can cause mental retardation in a human and CMV infects and/or replicates in a wide of variety of cell types, e.g., neurophils (see the left column of page 286).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular compounds of formula (1) of Protiva et al. in a method for treating CMV infection in a human.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular compounds of formula (1) of Protiva et al. in a method for treating CMV infection in a human, since these particular compounds

are known to have psychotropic and neurotropic activity and useful as neuroleptics according to Protiva et al. It is known that CMV infection is manifested by severe brain damage, CNS damage or CNS involvement in a human, according The Merck Manual of Diagnosis and Therapy, and it is also known that CMV infection can cause mental retardation in a human and CMV infects and/or replicates in a wide of variety of cell types, e.g., neurophils, according to Michelson.

Therefore, one of ordinary skill in the art would have reasonably expected that the particular compounds of formula (1) of Protiva et al. would have beneficial therapeutic effects in treating CMV infection in a human who suffers severe brain damage, CNS damage, or CNS disorders caused by CMV, since these compounds have psychotropic and neurotropic activity and useful as neuroleptics.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed on October 31, 2003 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant's arguments that "a psychotropic agent could be without effect, harmful, or beneficial with respect to the treatment of any particular CNS condition, including any CNS conditions associated with CMV infection, depends upon the therapeutic activity of the agent and the CNS condition. Thus, the teaching of an agent has psychotropic activity does nothing to indicate the particular condition(s) for which

the compounds would be beneficial" have been fully considered but are not deemed persuasive since the record contains no clear and convincing evidence of nonobviousness or unexpected results for the claimed method herein over the prior art. Examples 1-3 provide no clear and convincing evidence for treating CMV infection in a human. In this regard, it is noted that the specification provides no side-by-side comparison with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art. It is noted that arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., In re Huang, 100 F.3d 135,139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).

Therefore, one of ordinary skill in the art would have reasonably expected that the particular compounds of formula (1) of Protiva et al. would have beneficial therapeutic effects in treating CMV infection in a human who suffers severe brain damage, CNS damage, or CNS disorders caused by CMV, absent persuasive evidence.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

Claims 29-34 as amended now and new claims 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sindelar et al. (abstract, PTO-892) in view of in view of the Merck Manual of Diagnosis and Therapy (17th ED) (PTO-892) and Michelson ("AT", PTO-1449 submitted May 12, 2003).

Sindelar et al. discloses that the compounds of formula (I), octoclothepin and methiothepin in particular which are the instant preferred compounds in claims 30-34, and which are also known small organic compounds having a molecular weight of less than 800 daltons, have psychotropic and neurotropic activity and are useful as neuroleptics (see title and abstract).

Sindelar et al. does not expressly disclose the employment of the particular compounds in a method for treating CMV infection in a human, and wherein the chemokine is fractalkine.

The Merck Manual of Diagnosis and Therapy (17th ED) teaches that CMV infection is manifested by severe brain damage, CNS damage or CNS involvement in a human. See the right column of page 1295 to the left column of page 1296.

Michelson teaches that CMV infection can cause mental retardation in a human and CMV infects and/or replicates in a wide of variety of cell types, e.g., neurophils (see the left column of page 286).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular compounds of formula (1) of Sindelar et al. in a method for treating CMV infection in a human.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular compounds of formula (1) of Sindelar et al. in a method for treating CMV infection in a human, since these particular compounds are known to have psychotropic and neurotropic activity and useful as neuroleptics according to Protiva et al. It is known that CMV infection is manifested by severe brain

damage, CNS damage or CNS involvement in a human, according The Merck Manual of Diagnosis and Therapy, and it is also known that CMV infection can cause mental retardation in a human and CMV infects and/or replicates in a wide of variety of cell types, e.g., neurophils, according to Michelson.

Therefore, one of ordinary skill in the art would have reasonably expected that the particular compounds of formula (1) of Sindelar et al. would have beneficial therapeutic effects in treating CMV infection in a human who suffers severe brain damage, CNS damage, or CNS disorders caused by CMV, since these compounds have psychotropic and neurotropic activity and useful as neuroleptics.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed on October 31, 2003 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as already discussed above.

Therefore, one of ordinary skill in the art would have reasonably expected that the particular compounds of formula (1) of Sindelar et al. would have beneficial therapeutic effects in treating CMV infection in a human who suffers severe brain damage, CNS damage, or CNS disorders caused by CMV, since these compounds have psychotropic and neurotropic activity and useful as neuroleptics, absent persuasive evidence.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
January 5, 2004

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

1/12/04